UNITED STATES PATENT AND TRADEMARK OFFICE

UNITED STATES DEPARTMENT OF COMMERCE
United States Patent and Trademark Office
Address: COMMISSIONER OF PATENTS AND TRADEMARKS
Washington, D.C. 20231
www.uspto.gov

APPLICATION NO.	FILING DATE	FIRST NAMED INVENTOR	ATTORNEY DOCKET NO.	CONFIRMATION NO.
09/292,217	04/15/1999	STEPHEN D. GILLIES	LEX-004	3227

21323 7590 12/06/2001

TESTA, HURWITZ & THIBEAULT, LLP
HIGH STREET TOWER
125 HIGH STREET
BOSTON, MA 02110

EXAMINER
ROARK, JESSICA H

ART UNIT	PAPER NUMBER
1644	15

DATE MAILED: 12/06/2001

Please find below and/or attached an Office communication concerning this application or proceeding.

Office Action Summary	Application No. 09/292,217	Applicant(s) GILLIES, STEPHEN D.	
	Examiner Jessica H. Roark	Art Unit 1644	

-- The MAILING DATE of this communication appears on the cover sheet with the correspondence address --

Period for Reply

A SHORTENED STATUTORY PERIOD FOR REPLY IS SET TO EXPIRE 3 MONTH(S) FROM THE MAILING DATE OF THIS COMMUNICATION.

- Extensions of time may be available under the provisions of 37 CFR 1.136(a). In no event, however, may a reply be timely filed after SIX (6) MONTHS from the mailing date of this communication.
- If the period for reply specified above is less than thirty (30) days, a reply within the statutory minimum of thirty (30) days will be considered timely.
- If NO period for reply is specified above, the maximum statutory period will apply and will expire SIX (6) MONTHS from the mailing date of this communication.
- Failure to reply within the set or extended period for reply will, by statute, cause the application to become ABANDONED (35 U.S.C. § 133).
- Any reply received by the Office later than three months after the mailing date of this communication, even if timely filed, may reduce any earned patent term adjustment. See 37 CFR 1.704(b).

Status

1)☒ Responsive to communication(s) filed on *20 September 2001* .

2a)☐ This action is **FINAL**. 2b)☒ This action is non-final.

3)☐ Since this application is in condition for allowance except for formal matters, prosecution as to the merits is closed in accordance with the practice under *Ex parte Quayle*, 1935 C.D. 11, 453 O.G. 213.

Disposition of Claims

4)☒ Claim(s) *1-39* is/are pending in the application.

4a) Of the above claim(s) _____ is/are withdrawn from consideration.

5)☐ Claim(s) _____ is/are allowed.

6)☒ Claim(s) *1-39* is/are rejected.

7)☐ Claim(s) _____ is/are objected to.

8)☐ Claim(s) _____ are subject to restriction and/or election requirement.

Application Papers

9)☐ The specification is objected to by the Examiner.

10)☐ The drawing(s) filed on _____ is/are: a)☐ accepted or b)☐ objected to by the Examiner.

Applicant may not request that any objection to the drawing(s) be held in abeyance. See 37 CFR 1.85(a).

11)☐ The proposed drawing correction filed on _____ is: a)☐ approved b)☐ disapproved by the Examiner.

If approved, corrected drawings are required in reply to this Office action.

12)☐ The oath or declaration is objected to by the Examiner.

Priority under 35 U.S.C. §§ 119 and 120

13)☐ Acknowledgment is made of a claim for foreign priority under 35 U.S.C. § 119(a)-(d) or (f).

a)☐ All b)☐ Some * c)☐ None of:

1.☐ Certified copies of the priority documents have been received.

2.☐ Certified copies of the priority documents have been received in Application No. _____ .

3.☐ Copies of the certified copies of the priority documents have been received in this National Stage application from the International Bureau (PCT Rule 17.2(a)).

* See the attached detailed Office action for a list of the certified copies not received.

14)☒ Acknowledgment is made of a claim for domestic priority under 35 U.S.C. § 119(e) (to a provisional application).

a) ☐ The translation of the foreign language provisional application has been received.

15)☐ Acknowledgment is made of a claim for domestic priority under 35 U.S.C. §§ 120 and/or 121.

Attachment(s)

1) ☐ Notice of References Cited (PTO-892)
2) ☐ Notice of Draftsperson's Patent Drawing Review (PTO-948)
3) ☒ Information Disclosure Statement(s) (PTO-1449) Paper No(s) *14* .
4) ☐ Interview Summary (PTO-413) Paper No(s). _____ .
5) ☐ Notice of Informal Patent Application (PTO-152)
6) ☐ Other: .

RESPONSE TO APPLICANT'S AMENDMENT

1. A request for continued examination under 37 CFR 1.114, including the fee set forth in 37 CFR 1.17(e), was filed in this application after final rejection. Since this application is eligible for continued examination under 37 CFR 1.114, and the fee set forth in 37 CFR 1.17(e) has been timely paid, the finality of the previous Office action has been withdrawn pursuant to 37 CFR 1.114. Applicant's submission filed on 9/20/01 has been entered.

2. Applicant's amendment, filed 9/20/01 (Paper No. 13), is acknowledged.
Claims 1-3, 8, 12, 17, 20, 23, 27, 31 and 36 have been amended.
Claims 1-39 are pending and being acted upon presently.

3. Provisional application 60/081,863 appears to provide adequate written support for the instant claims.

4. Applicant's IDS, filed 9/20/01 (Paper No. 14), is acknowledged.

5. Formal drawings have been submitted which fail to comply with 37 CFR 1.84.
Please see the form PTO-948 attached previously to Paper No. 8.

6. The lengthy specification has not been checked to the extent necessary to determine the presence of all possible minor errors. Applicant's cooperation is requested in correcting any errors of which Applicant may become aware in the specification.

7. The text of those sections of Title 35 USC not included in this Action can be found in a prior Action.
This Office Action will be in response to Applicant's arguments, filed 9/20/01 (Paper No. 13).
The rejections of record can be found in the previous Office Action (Paper Nos. 8 and 10).

It is noted that New Grounds of Rejection are set forth herein.

8. The Non-statutory double patenting rejection set forth in Paper No. 8 is held in abeyance.

9. The following is a quotation of the first paragraph of 35 U.S.C. 112:

The specification shall contain a written description of the invention, and of the manner and process of making and using it, in such full, clear, concise, and exact terms as to enable any person skilled in the art to which it pertains, or with which it is most nearly connected, to make and use the same and shall set forth the best mode contemplated by the inventor of carrying out his invention.

10. Claim 3 is rejected under 35 U.S.C. 112, first paragraph, as containing subject matter which was not described in the specification in such a way as to enable one skilled in the art to which it pertains, or with which it is most nearly connected, to make and/or use the invention.

Instant claim 3 recites a method of inducing a cytocidal response against a virus-infected cell by administering a combination of an immunoconjugate and an angiogenesis inhibitor, wherein the combination induces a cytocidal immune response against the virus-infected cell that is greater than the response induced by the immunoconjugate alone.

The art at the time the invention was made recognized the application of immunoconjugates comprising certain cytokines in methods of targeting virus-infected cells for lysis (e.g., Gillies, WO92/08495, IDS #BA). Further, angiogenesis inhibitors were well known in the art at the time the invention was made for use as inhibitors of tumor growth and metastases because of their ability to block angiogenesis essential for tumor growth (e.g., O'Reilly et al. Cell 88:277-285 1997, IDS #CV; O'Reilly et al. 1994 Cell 79:315-328 1994, IDS # CU; Brooks et al. Cell 79:1157-1164 1994, IDS #CC; or Ingber et al. Nature 348:555-557 1990, IDS # CM). However, there does not appear to be any recognized association between angiogenesis inhibitors and elimination of a virus-infected cell. Thus the state of the art does not appear to recognize that the addition of an angiogenesis inhibitor to an immunoconjugate would induce a greater cytocidal immune response against a virus-infected cell than would the immunoconjugate alone. Neither does Applicant appear to provide any working examples providing objective evidence that a combination comprising an immunoconjugate and an angiogenesis inhibitor could induce a greater cytocidal immune response against a virus-infected cell than the immunoconjugate alone. Thus the skilled artisan did not recognize that an angiogenesis inhibitor could be applied in the instant method, and would consider the instant method to be highly unpredictable in the absence of objective evidence. Given this unpredictability; the experimentation left to those skilled in the art to use the instant method is unnecessarily, and improperly, extensive and undue.

11. Claims 1-2 and 4-39 are rejected under 35 U.S.C. 103(a) as being unpatentable over Gilles et al. (WO 92/08495, IDS #BA), in view of O'Reilly et al. (Cell 88:277-285 1997, IDS # CV).

Applicant's arguments, filed 9/20/01 (Paper No. 13), have been fully considered, but have not been found convincing essentially for the reasons of record set forth in Paper Nos. 8 and 12.

Applicant argues that the newly added limitation requiring that the cytocidal response against the target cell be greater than the response induced by the immunoconjugate alone overcomes the rejection of record. Applicant also again argues that the instant claims differ from the teachings of the references in that O'Reilly's suggestion of a combined treatment for tumor therapy is directed only to the teachings of Teicher et al. (Int. J. Cancer 1994; 57:1-6, IDS #CAG) which address DNA-targeting agents resulting in cell death, for use in combined therapy with an antiangiogenic agent.

As previously noted in Paper No. 12, it is clear in O'Reilly et al. from the text preceding the phrase "cytotoxic chemotherapy" on page 282 at lines 26-27 that any agent that "selectively or specifically" targets the tumor cell population was appropriate to combine with the angiogenesis inhibitor taught by O'Reilly et al. (page 282, 1st full paragraph, 2nd column). The immunoconjugate taught by Gilles et al., as well as the immunoconjugate of the instant disclosure, are each agents that "selectively and specifically" target tumor cells. In addition, the advantages offered by a selective therapeutic agent, versus the highly unselective standard cytotoxic chemotherapy, were appreciated by the ordinary artisan. Thus it would have been obvious to the ordinary artisan at the time the invention was made to substitute the specific cytocidal immunoconjugate taught by Gilles et al. in any therapy involving cellular cytotoxicity.

Applicant is again reminded that specific statements in the references themselves which would spell out the claimed invention are not necessary to show obviousness, since questions of obviousness involves not only what references expressly teach, but what they would collectively suggest to one of ordinary skill in the art. See CTS Corp. v. Electro Materials Corp. of America 202 USPQ 22 (DC SNY); and In re Burckel 201 USPQ 67 (CCPA).

With respect to the newly added limitation that the cytocidal response against the target cell be greater than the response induced by the immunoconjugate alone; it was well known in the art that the expected result of combination therapy is that the combination would function more effectively than the individual components. Indeed, the strongest rationale for combining references is a recognition, expressly or impliedly in the prior art or drawn from a convincing line of reasoning based on established scientific principles or legal precedent, that some advantage or expected beneficial result would have been produced by their combination. In re Sernaker, 217 USPQ 1, 5 - 6 (Fed. Cir. 1983). In the instant case, the teachings of the references clearly indicated, as noted supra, that the cytocidal response against the target cell would be greater if an agent targeting a tumor cell for lysis and an angiogenesis inhibitor were combined.

Thus Applicant's arguments with respect to the instant claims are not found persuasive.
The rejection is maintained

12. Claims 1, 11, and 26 are rejected as being unpatentable over Gillies (WO 92/08495, IDS # BA) in view of O'Reilly et al. 1994 (Cell 79:315-328 1994, IDS # CU) or Brooks et al. (Cell 79:1157-1164 1994, IDS #CC) or Ingber et al. (Nature 348:555-557 1990, IDS# CM).

Applicant argues that Gillies has been addressed supra with respect to the newly added limitations, and that none of O'Reilly et al. 1994, Brooks et al., or Ingber et al. cure the deficiencies of Gillies.

As discussed supra and pointed out previously in Paper Nos. 8 and 12, the ordinary artisan clearly appreciated that therapies targeting both the tumor and endothelial population could be beneficially combined with any specific forms of angiogenesis inhibitors. An expected beneficial result of a combination therapy is that the response induced is greater than that of either component.

Applicant is again reminded that the strongest rationale for combining references is a recognition, expressly or impliedly in the prior art or drawn from a convincing line of reasoning based on established scientific principles or legal precedent, that some advantage or expected beneficial result would have been produced by their combination. In re Sernaker, 217 USPQ 1, 5 - 6 (Fed. Cir. 1983).

Applicant's arguments are not found persuasive.
The rejection is maintained.

13. No claim allowed

14. Any inquiry concerning this communication or earlier communications from the examiner should be directed to Jessica H. Roark, whose telephone number is (703) 605-1209. The examiner can normally be reached Monday to Friday, 8:00 to 4:30. A message may be left on the examiner's voice mail service. If attempts to reach the examiner by telephone are unsuccessful, the examiner's supervisor, Christina Chan can be reached at (703) 308-3973. Any inquiry of a general nature or relating to the status of this application should be directed to the Technology Center 1600 receptionist whose telephone number is (703) 308-0196.

Papers related to this application may be submitted to Technology Center 1600 by facsimile transmission. Papers should be faxed to Technology Center 1600 via the PTO Fax Center located in Crystal Mall 1. The faxing of papers must conform with the notice published in the Official Gazette, 1096 OG 30 (November 15, 1989). The CM1 Fax Center telephone number is (703) 305-3014.

Jessica Roark, Ph.D.
Patent Examiner
Technology Center 1600
December 5, 2001

PHILLIP GAMBEL, PH.D
PRIMARY EXAMINER
TECH CENTER 1600
12/5/01